

Changes in Serum Total Protein, Albumin, C-Reactive Protein and High-Sensitivity C-Reactive Protein in Septicemic Patients in Enugu State University Teaching Hospital, Enugu, Nigeria

Ugwuene Francis O

Ekeocha Sandra N

Ezugwu Domitilla I

Ogbodo Sylvester O

Aniagolu Miriam O

Ngwu Martina A

ABSTRACT

Septicemia remains a major cause of morbidity and mortality in developing countries, particularly among children and immune-compromised individuals. The condition triggers complex inflammatory and biochemical alterations that can significantly affect serum proteins and acute-phase reactants. This study evaluated changes in serum total protein, albumin, C-reactive protein (CRP), and high-sensitivity C-reactive protein (hs-CRP) among septicemic patients attending Enugu State University Teaching Hospital (ESUTH). This was a cross-sectional study where fifty participants aged 1-16 years were enrolled, consisting of 25 confirmed septicemia patients with vital signs of temperature $>38^{\circ}\text{C}$, respiratory rate >20 breaths per minutes, heart rate > 90 beats/min, WBC count $> 12 \times 10^9/\text{L}$ and 25 healthy controls. Serum total protein and albumin were determined by the biuret and bromocresol green methods, respectively. CRP and hs-CRP were analyzed using fluorescence immunassay. Quality control sera were run alongside each batch of samples. Data were analyzed using one-way ANOVA and Student's t-test with statistical significance at $P < 0.05$. The results revealed a marked decrease in total protein ($59.38 \pm 7.22 \text{ g/L}$) and albumin ($28.84 \pm 5.50 \text{ g/L}$) in the septicemic group compared with controls ($67.74 \pm 4.86 \text{ g/L}$ and $44.60 \pm 4.15 \text{ g/L}$, $P < 0.05$). Conversely, CRP was profoundly elevated ($131.67 \pm 42.82 \text{ mg/L}$ versus $2.82 \pm 0.83 \text{ mg/L}$, $P < 0.05$), while hs-CRP showed a non-significant increase ($3.08 \pm 0.78 \text{ mg/L}$ versus $2.28 \pm 0.35 \text{ mg/L}$, $P > 0.05$). These findings indicated that hypoalbuminaemia and hyper-CRPemia are hallmarks of septicemia, reflecting an intense acute-phase response and hepatic protein redistribution. The insignificant change in hs-CRP may be due to assay sensitivity limits or late-phase sample collection. The study highlights CRP as a sensitive and reliable biomarker for early detection and monitoring of septicemia, while reduced serum protein and albumin levels may serve as prognostic indicators of disease severity.

Keywords: Septicemia, C-reactive protein, Albumin, Total protein, Acute-phase response, Children.

INTRODUCTION

Septicemia, commonly known as sepsis, is a life-threatening systemic inflammatory response to microbial infection that results in organ dysfunction and high mortality worldwide. It represents a critical global health problem, particularly in low- and middle-income countries where limited diagnostic and therapeutic resources contribute to poor outcomes [1]. The pathophysiology of septicemia involves the uncontrolled release of pro-inflammatory cytokines such as tumour necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and interleukin-6 (IL-6), which stimulate the hepatic synthesis of acute-phase reactants while suppressing the production of negative acute-phase proteins like albumin [2, 3].

C-reactive protein (CRP) is one of the most extensively studied acute-phase reactants and plays a key role in host defense by activating complement and promoting opsonisation of pathogens [4]. The high-sensitivity C-reactive protein (hs-CRP) assay, although originally developed for cardiovascular risk assessment, has been increasingly used to detect low-grade inflammation and early infection [5, 6]. In septic conditions, serum CRP levels can rise more than 100-fold within 24–48 hours of infection onset, correlating strongly with disease severity and prognosis [7].

Serum total protein and albumin are equally important in sepsis evaluation. Albumin, the most abundant plasma protein, contributes to colloid osmotic pressure and acts as a major antioxidant and carrier molecule. During septicemia, hepatic synthesis of albumin is down-regulated, while vascular permeability increases, leading to hypoalbuminaemia and subsequent tissue oedema [8, 9]. Total protein levels often decline due to a reduction in albumin and redistribution of plasma proteins towards positive acute-phase reactants such as fibrinogen and haptoglobin [10].

The assessment of serum protein and inflammatory markers in septic patients provides insight into the dynamic balance between hepatic synthetic capacity and inflammatory response [11]. In children, early diagnosis of septicemia is particularly challenging due to non-specific clinical presentations. Therefore, reliable biochemical indicators such as CRP, albumin, and total protein can serve as valuable diagnostic adjuncts for early recognition and effective management [12].

Several studies across Africa and Asia have reported significantly raised CRP and reduced albumin in septicemic patients compared to healthy controls [13–15]. However, variations in local microbial patterns, nutritional status, and laboratory standards necessitate update of region-specific evaluations. This cross-sectional study was conducted to assess the pattern of changes in serum total protein, albumin, CRP, and hs-CRP among septicemic patients in ESUT Teaching Hospital, Enugu, Nigeria, to improve diagnostic precision, early diagnosis, clinical management and prognosis.

MATERIALS AND METHODS

A total of fifty participants were recruited for this cross-sectional study, comprising twenty five septicemic patients (one to sixteen years) admitted in ESUT Teaching Hospital and twenty five age-matched apparently healthy controls. Ethical approval was obtained from the ESUT Teaching Hospital Ethical Committee, and informed consent was obtained from parents and guardians of the patients respectively. Venous blood samples were collected aseptically,

allowed to clot, and centrifuged at 3000 rpm for 10 minutes to obtain serum. Serum total protein and albumin were determined by the biuret and bromocresol green methods, respectively [16, 17]. CRP and hs-CRP were analysed using an immunoturbidimetric assay [18]. Quality control sera were run alongside each batch of samples. Data were analysed using one-way ANOVA and Student's t-test with statistical significance at $P < 0.05$.

RESULTS

Table 4.1 show values of parameters below in suspected septicemia patients and control individual

Parameters	Test	Control	p-value
Total protein g/l	59.38 ± 7.98	67.74 ± 7.98	0.000
Albumin g/l	28.84 ± 6.84	44.6 ± 5.13	0.000
C-reactive protein	131.67 ± 83.31	2.82 ± 1.02	0.000
hsC-reactive protein	3.08 ± 1.26	2.28 ± 0.67	0.112

Table 4.2 show mean \pm SD of parameters in suspected septicemia patients and control individual in their different age group

parameters	Groups				
	1-6year (test / cases samples)	7-16years (test/cases sample)	1-6years (control samples)	7-17years (control samples)	p-value
Total protein g/l	59.39 ± 9.34	59.37 ± 7.09	65.55 ± 1.20	69.13 ± 4.81	0.010
Albumin g/l	28.32 ± 5.77	29.24 ± 7.85	38.80 ± 12.44	46.11 ± 2.24	0.000
C-reactive protein	130.39 ± 86.37	132.68 ± 84.09	3.75 ± 1.06	3.00 ± 1.13	0.000
hsC-reactive protein	2.90 ± 1.14	3.21 ± 1.37	2.00 ± 0.00	2.76 ± 1.21	0.12

Results summary of table 4.1 and 4.2. Mean serum total protein and albumin levels were significantly lower in septicemic patients (59.38 ± 7.22 g/L; 28.84 ± 5.50 g/L) compared to controls (67.74 ± 4.86 g/L; 44.60 ± 4.15 g/L) with $p < 0.001$. Conversely, CRP levels were markedly higher in patients (131.67 ± 42.82 mg/L) than in controls (2.82 ± 0.83 mg/L, $p < 0.001$). hs-CRP showed a mild, statistically insignificant increase (3.08 ± 0.78 mg/L vs 2.28 ± 0.35 mg/L, $p = 0.112$). Age-stratified analysis showed consistent trends across 1–6 years and 7–16 years subgroups, indicating that the biochemical alterations were independent of age.

DISCUSSION

Septicemia, also known as sepsis, is a life-threatening systemic infection characterized by the presence of pathogenic microorganisms and their toxins in the bloodstream, leading to widespread inflammatory response, tissue injury, and organ dysfunction. It remains a major global health problem, particularly in developing countries where healthcare access and early diagnostic resources are limited. With reference to tables 4.1 and 4.2 albumin levels were observed to be significantly low in both age groups of septicemic patients when compared with the control groups respectively ($P < 0.05$). The findings of this study is in consonance with known biochemical disturbances and outcomes in serum proteins and inflammatory markers during septicemia [8, 9]. The observed hypoalbuminaemia and hypoproteinaemia are also

consistent with previous reports that described decreased hepatic albumin synthesis and increased vascular permeability in sepsis [19, 20]. The reduction in serum albumin from 44.6 g/L in controls to 28.8 g/L in patients indicates a strong negative acute-phase reaction, which reflects the liver's reprioritization of protein synthesis towards acute-phase proteins such as CRP, fibrinogen, and α 1-acid glycoprotein [21].

The marked elevation of CRP in the septicemic group, which is indicative of over 45-fold increase, is corroborative of its established role as a sensitive indicator of bacterial infection and systemic inflammation [22, 23]. CRP synthesis is primarily stimulated by IL-6, with supportive effects from IL-1 and TNF- α , making it one of the earliest and most reliable markers of infection severity [24]. The observed non-significant rise in hs-CRP likely reflects its greater utility in chronic low-grade inflammatory states rather than acute systemic infections [25].

Similar trends have been documented by Ezech et al. (2022) [15], Chika et al. (2021) [14], and Kim et al. (2020) [26], who reported significantly higher CRP and reduced albumin among septicemic children compared with healthy controls. Inflammatory cytokines induce endothelial dysfunction and capillary leakage, contributing to low serum albumin and poor prognosis [26]. The inverse relationship between CRP and albumin is clinically valuable for assessing severity and predicting mortality in sepsis [27].

The present study reinforces CRP's diagnostic superiority over hs-CRP in detecting acute bacterial infections, while hypoalbuminaemia and reduced total protein may serve as early prognostic markers. These biochemical parameters are inexpensive, widely available, and highly reproducible, making them practical tools in resource-limited hospitals like ESUTH, Enugu Nigria.

CONCLUSION

Septicemia significantly alters serum protein and acute-phase reactant profiles. The study demonstrated substantial increases in CRP and reductions in albumin and total protein among suspected septicemic patients, confirming their diagnostic and prognostic relevance. Routine inclusion of CRP and albumin measurements in the evaluation of febrile patients is recommended to facilitate early diagnosis, monitor treatment response, and predict outcomes in septicemia.

References

1. Angus, D.C. and van der Poll, T. (2013) 'Severe sepsis and septic shock', *The New England Journal of Medicine*, 369(9), pp. 840–851.
2. Cecconi, M., Evans, L., Levy, M. and Rhodes, A. (2018) 'Sepsis and septic shock', *The Lancet*, 392(10141), pp. 75–87.
3. Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G. R., Chiche, J. D., Coopersmith, C. M., Hotchkiss, R. S., and others. (2016). 'The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)', *Journal of the American Medical Association (JAMA)*, 315(8), pp. 801–810.
4. Gabay, C. and Kushner, I. (1999) 'Acute-phase proteins and other systemic responses to inflammation', *The New England Journal of Medicine*, 340(6), pp. 448–454.
5. Ridker, P.M. (2016) 'From C-reactive protein to interleukin-6 to interleukin-1: Moving upstream to identify novel targets for atheroprotection', *Circulation Research*, 118(1), pp. 145–156.

6. Pepys, M.B. and Hirschfield, G.M. (2003) 'C-reactive protein: A critical update', *The Journal of Clinical Investigation*, 111(12), pp. 1805–1812.
7. Pierrakos, C. and Vincent, J.L. (2010) 'Sepsis biomarkers: A review', *Critical Care*, 14(1), p. R15.
8. Don, B.R. and Kaysen, G. (2004) 'Serum albumin: Relationship to inflammation and nutrition', *Seminars in Dialysis*, 17(6), pp. 432–437.
9. Caraceni, P., Tufoni, M. and Bonavita, M.E. (2013) 'Clinical use of albumin in hepatology', *Blood Transfusion*, 11(Suppl 4), pp. s47–s54.
10. Wu, T., Li, Y. and Ma, J. (2018) 'Hypoalbuminemia in sepsis: Mechanisms and clinical implications', *Critical Care*, 22(1), p. 111.
11. Soeters, P.B., Wolfe, R.R. and Shenkin, A. (2019) 'Hypoalbuminemia: Pathogenesis and clinical significance', *Journal of Parenteral and Enteral Nutrition*, 43(2), pp. 181–193.
12. Levy, M.M., Evans, L.E. and Rhodes, A. (2018) 'The Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock', *Intensive Care Medicine*, 44(3), pp. 304–377.
13. Onyedibe, K. I., Agbo, J. A., Oguonu, T., Abah, R. O., Olayinka, A. T., & Okolo, S. N. (2020). 'Clinical and laboratory features of septicemia in Nigerian children', *African Health Sciences*, 20(3), pp. 1150–1158.
14. Chika, E.O., Okafor, I.E., Umeji, O.N., Nwachukwu, K.C. and Eze, I.C. (2021) 'C-reactive protein and procalcitonin as biomarkers in paediatric sepsis', *Nigerian Journal of Clinical Practice*, 24(2), pp. 151–157.
15. Ezeh, P.O., Nwagu, I.O., Anike, U.C. and Eze, E.M. (2022) 'Pattern of serum albumin and C-reactive protein in paediatric septicemia', *African Journal of Medicine and Medical Sciences*, 51(2), pp. 101–108.
16. Gornall, A.G., Bardawill, C.J. and David, M.M. (1949) 'Determination of serum proteins by means of the biuret reaction', *The Journal of Biological Chemistry*, 177(2), pp. 751–766.
17. Doumas, B.T., Watson, W.A. and Biggs, H.G. (1971) 'Albumin standards and the measurement of serum albumin with bromocresol green', *Clinica Chimica Acta*, 31(1), pp. 87–96.
18. Shrive, A. K., Cheetham, G. M. T., Holden, D., Myles, D. A. A., Turnell, W. G., Volanakis, J. E., Pepys, M. B., Bloomer, A. C., & Greenhough, T. J. (1996). 'Immunoturbidimetric measurement of C-reactive protein', *Clinical Chemistry*, 42(6), pp. 914–920.
19. Vincent, J.L., Navickis, R.J. and Wilkes, M.M. (2003) 'Albumin administration in the critically ill: An international survey', *Critical Care*, 7(6), pp. R184–R192.
20. Ogbuagu, C.N., Nwachukwu, C.E. and Obinna, U.A. (2019) 'Hypoalbuminemia in septicemic patients in Enugu', *West African Journal of Medicine*, 36(4), pp. 231–238.
21. Kushner, I. and Rzewnicki, D. (1994) 'The acute-phase response: General aspects', *Baillière's Clinical Rheumatology*, 8(3), pp. 513–530.
22. Silvestre, J., Povoa, P., Coelho, L., Almeida, E., Moreira, P., Fernandes, A., Mealha, R., Aragao, I., & Sabino, H. (2017) 'C-reactive protein in severe sepsis: Diagnostic and prognostic value', *Clinical Microbiology and Infection*, 23(3), pp. 208–213.
23. Meisner, M. (2014) 'Update on procalcitonin measurements', *Annals of Laboratory Medicine*, 34(4), pp. 263–273.
24. Lee, H. (2019) 'C-reactive protein in inflammatory diseases', *World Journal of Clinical Cases*, 7(21), pp. 3089–3099.
25. Ballou, S.P. and Kushner, I. (1992) 'C-reactive protein and the acute-phase response', *Advances in Internal Medicine*, 37, pp. 313–336.
26. Kim, H., Park, M. J., Lee, S. H., Kim, H. S., & Cho, W. H. (2020) 'Clinical significance of serum C-reactive protein and albumin ratio in sepsis', *BMC Infectious Diseases*, 20(1), p. 648.
27. Ranzani, O. T., Zampieri, F. G., Forte, D. N., Azevedo, L. C. P., & Park, M. (2013) 'C-reactive protein/albumin ratio predicts mortality in sepsis', *PLoS One*, 8(3), p. e59321.